

Inventors: ~~C~~ et al.  
Serial No.: 10/021,906  
Filed: December 12, 2001  
Page 2

In the specification:

At page 1, delete the first paragraph and substitute therefor:

B1

This application is continuation of U.S. Serial No. 09/517,945, filed March 3, 2000, now U.S. Patent 6,355,431, issued March 12, 2002, which claims benefit of U.S. Provisional Application No. 60/160,927, filed October 22, 1999, now abandoned, U.S. Provisional Application No. 60/161,148, filed October 22, 1999, now abandoned, U.S. Provisional Application No. 60/160,917, filed October 22, 1999, now abandoned, U.S. Provisional Application No. 60/135,051, filed May 20, 1999, U.S. Provisional Application No. 60/135,053, filed May 20, 1999, U.S. Provisional Application No. 60/135,123, filed May 20, 1999, and U.S. Provisional Application 60/130,089, filed April 20, 1999. ~~The present invention is a continuation in part of U.S.S.N. 60/161,148, filed October 22, 1999, which is a continuation in part of U.S.S.N. 60/135,051, filed May 20, 1999, and a continuation in part of U.S.S.N. 60/160,027, filed October 22, 1999, which is a continuation in part of U.S.S.N. 60/130,089, filed April 20, 1999, all of which are pending.~~

fourth

At page 7, delete the ~~third~~ full paragraph, and substitute therefor:

B2

Figure 4 depicts a preferred embodiment of the invasive cleavage reaction. In this embodiment, the

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CDU-4

signaling probe 65 comprises two portions, a detection sequence 67 and a signaling portion 66. A second distinct probe 70 for invasive cleavage is also known as an invade probe. The signaling portion can serve as an adapter sequence. In addition, the signaling portion generally comprises the label 55, although as will be appreciated by those in the art, the label may be on the detection sequence as well. In addition, for optional removal of the uncleaved probes, a capture tag 60 may also be used. Upon addition of the enzyme, the structure is cleaved, releasing the signaling portion 66. The reaction can be repeated and then the signaling portion is added to the array as above.

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~~sixth~~

At page 7, delete the ~~fifth~~ full paragraph bridging pages 7 and 8, and substitute therefor:

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B3

Figure 6 depicts OLA/RCA amplification using a single "padlock probe" 57. Figure 6A shows the ~~[[The]]~~ padlock probe ~~[[is]]~~ hybridized with a target sequence 25. When the probe 57 is complementary to the target sequence 26, ligation of the probe termini occurs forming a circular probe 28. When the probe 57 is not complementary to the target sequence 27, ligation does not occur. Addition of polymerase and nucleotides to the circular probe results amplification of the probe 58. Figure 6B shows cleavage ~~[[Cleavage]]~~ of the amplification probe 58 yields fragments 59 that hybridize with an identifier probe 21 immobilized on a microsphere 10.

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At page 8, delete the first full paragraph, and substitute therefor:

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B4

Figure 7 depicts an alternative method of OLA/RCA. Figure 7A-C shows an [[An]] immobilized first OLA primer 45 is hybridized with a target sequence 25 and a second OLA primer 50. Following the addition of ligase, the first and second OLA primers are ligated to form a ligated oligonucleotide 56. Figure 7D shows that following ~~[[Following]]~~ denaturation to remove the target nucleic acid, the immobilized ligated oligonucleotide is distributed on an array. Figure 7E-F shows an ~~[[An]]~~ RCA probe 57 and polymerase ~~[[are]]~~ added to the array resulting in amplification of the circular RCA probe 58.

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